

APPENDIX B

| Claim Limitation | Support in Adair Application |
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| 24. A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from human acceptor immunoglobulin heavy and light chains | See page 1, lines 5-16, and page 7, line 32, through page 8, line 21. |
| which humanized immunoglobulin specifically binds to an antigen with an affinity constant of at least 10^8 M^{-1} . | See page 11, lines 27-30. |
| wherein said humanized immunoglobulin comprises amino acids from the donor immunoglobulin framework outside both the Kabat CDRs and the structural loop CDRs of the variable regions, | See page 6, lines 14-23, page 8, lines 13-16, and page 19, line 16, to page 20, line 15. |
| wherein the donor amino acids replace corresponding amino acids in the acceptor immunoglobulin heavy or light chain frameworks, | See page 6, line 12, to page 7, line 5. |
| and each of said donor amino acids is adjacent to a CDR in the donor immunoglobulin sequence | See page 11, lines 16-20, showing that homology is maximized between donor and acceptor sequences adjacent CDRs within acceptor framework. At page 6, lines 25-35, it is indicated that the heavy chain "framework comprises donor residues at at least one of positions 6, 23 and/or 24, 48 and/or 49...." In the heavy chain, Kabat CDR2 together with [Chothia] structural loop H2 extends from residues 50 to 65. Thus, residue 49 is immediately adjacent the beginning of this CDR2/H2 region. |

or contributes to antigen binding as determined by X-ray crystallography.

Page 38, lines 1-12, and lines 23-38, and Figs. 3-4 of the application as filed reference residues that may "contribute to antigen binding" as determined using X-ray crystallography. Residues 6, 23,24, and 48 are identified in Figure 4.